

positions.

(i). Applicants formally traverse the Restriction Requirement as presented by the Examiners for the reasons stated below; and

(ii). Applicants provisionally elect to prosecute claims 11-15 respectively, Group V, drawn to a family of PR-39 derived oligopeptides which cause an inhibition of proteasome-mediated degradation in-situ after introduction to a viable cell.

REMARKS

1. Applicants respectfully submit that the Examiners' demand for a Restriction Requirement under 35 U.S.C. 121 at this time is both legally untimely, procedurally inappropriate, and blatantly unfair. The present invention as now defined by claims 1-15 collectively has been actively considered and prosecuted as a single, integrated invention for more than one year's time; has been the subject of multiple reviews on the merits as a unitary invention by the prior Patent Examiner of record as shown by two different non-final Official Actions; and now includes, as a matter of formal record, two separately filed Responses which presented facts, law and argument in reply to each prior Official Action upon the basis that a single integrated invention was being evaluated on the merits. It is unequivocally demonstrated, therefore, that throughout the entirety of the prosecution to date, applicants' invention was considered,

reviewed and evaluated repeatedly as a single unitary invention by the prior Patent Examiner of record.

Moreover, as evidenced by the prosecution file history of record to date, applicants have substantially amended the wording of the claims now pending - which now differ markedly from the language of the originally submitted claims. Such claim amendment as has occurred to date was made, in major degree, in consideration of applicants' claimed invention being considered by the prior Patent Examiner as one single entity and a unitary whole; and the pending claims were individually amended as part of each filed Response with respect to the language and wording of one another - in order to reflect their mutual co-pending existence as alternative, but complimentary, recitations which cumulatively and collectively define the true scope of applicants' subject matter as a whole broadly.

Now surprisingly, and for reasons unknown to applicants and their undersigned attorney, the instant application appears to have been formally transferred from the custody of the prior Patent Examiner (F.T. Moezie) to the custody of the present Examiners (Messrs. Kam & Low). This case transfer is in itself is unaccounted for and remains unexplained.

What is clearly inappropriate and improper, however, is that the present Examiners have apparently refused to recognize or consider the lengthy prosecution history to date for the instant application. It appears

that the present Examiners have not bothered to examine the prosecution file history to date for the instant application; and instead chosen to treat the presently pending claims as if such claims were the originally submitted definitions and were never considered or reviewed on the merits at all.

Applicants respectfully affirm that Messrs. Kam & Low cannot treat the instant application as if the presently pending claims were totally new and previously unexamined original claims; nor can the Examiners pretend that the presently pending claims were not twice previously reviewed on the merits via different Official Actions of record; nor can the Examiners overlook and ignore the legal precedent value and substantive effects of the lengthy prosecution history of record to date, both legally and factually, as if such a prosecution history did not really exist.

Applicants maintain, therefore, that the present Examiners must accept and be bound by the entirety of the prosecution file history to date for what it actually is; and must also come to recognize that their instant demand for Restriction of and Election among the presently pending claims is legally inequitable as well as procedurally improper. In addition, applicants submit that the present Examiners of record, Messrs. Kam & Low, are legally prevented and equitably estopped by the substantive prosecution history to date for the presently pending claims from imposing a Restriction and Election Requirement at this time.

2. Applicants respectfully submit and maintain that all of claims 1-15 respectively now pending constitute a single and unitary invention; and define an integrated subject matter constituting one individual invention having multiple formats. The subject matter as a whole comprising applicants' integrated invention is defined in the alternative by claims 1-10 and claims 11-15 respectively. Claims 1-10 collectively define a broad methodology while claims 11-15 define a composition of matter comprising a family of pharmacologically active oligopeptides intended for use in the methodology recited by claims 1-10.

The Examiners will note and appreciate that amended independent claim 1 is directed to a method for stimulating angiogenesis within a targeted collection of viable cells in-situ; whereas amended independent claim 2 defines a method for altering proteosome-mediated degradation of peptides within a collection of viable cells. As presently stated, independent method claims 1 and 2 are similar in the limitations and requirements recited by their individual manipulative steps. Each method claim identifies a collection of cells in-situ as the target; provides means for introducing at least one member selected from the group consisting of the PR-39 oligopeptide collective to the cytoplasm of the targeted cells; introduces at least one member of the PR-39 oligopeptide

collective to the targeted cells; and then explicitly requires that the introduced PR-39 oligopeptide member interact with such proteasomes as are present within the cytoplasm of the targeted cells in three specified ways. Thus, as presently worded, claims 1 and 2 represent alternative definitions of reciting and for practicing a single, but broadly applied methodology; and claims 3-10 respectively depend from each of these independent claims and merely represent detailed embodiments of method claims 1 or 2 in an intimate and direct relationship.

Similarly, composition claims 11-15 are alternative recitations for the family of PR-39 derived oligopeptides whose members individually are able to cause an inhibition of proteasome-mediated degradation of at least one identifiable peptide in-situ after intracellular introduction to a viable targeted cell. This family of substances is defined most broadly by independent claims 11 and 15 respectively; and is more narrowly defined in detail by dependent claims 12-14 respectively.

All of pending claims 1-15 thus constitute a single invention defined in the alternative; and provides both broader and narrower delineations of operative methods as well as one particular family of PR-39 derived oligopeptides directed to and concerning one goal and objective – an inhibition of proteasome-mediated degradation. It will be noted also that each of method claims 1-10 requires the introduction of a PR-39 oligopeptide collective member, which can include those compositions

defined by claims 11-15, to the cytoplasm of the targeted cells; requires an interaction between the introduced PR-39 oligopeptide collective member and such proteasomes as are present intracellularly; and requires that the consequence of such interaction be a marked inhibition of proteolytic degradation activity.

Clearly, all of the presently pending claims are intimately related to each other; all commonly share the same essential features and requisite interactions, regardless of particular format; and all share a single inventive concept and basis, regardless of the incidental details recited within the individual independent claims. The entirety of claims 1-15 thus constitute a single unitary invention.

3. The present Examiners unfortunately appear to have been mislead and distracted by the alternative wording in the preamble of independent claims 1 and 2; and have not recognized or acknowledged the substantive commonality shared method claims 1 and 2 respectively. Applicants respectfully submit and maintain that methods claims 1 and 2 do not have different objectives; and do not employ different modes of operation; and do not perform meaningfully different functions; and do not utilize meaningfully different steps to achieve different effects. To the contrary, method claims 1 and 2 recite a single broadly recited process, the results and consequences of which proceed sequentially and are

defined in parallel, yet all of which originate from a common set of specified manipulative steps.

The Examiners have also stated that the methods defined by claim 1 and 2 would require separate searches of different technical fields. Applicants respectfully submit that this view and position is erroneous in every respect. Contrary to the Examiners' speculation, there is only one broad invention which commonly employs similar manipulations and compositions in combination to achieve a series of specified results and beneficial consequences. Each result and consequence recited by claims 1 and 2 individually is the outcome of the same broad methodology and technique. Thus, only one co-extensive search in the same technical field, whether carried out by computer or by hand, would be needed; and only one search effort by the Examiners need be made in order to identify the relevant and material prior art relevant for applicants' unitary invention.

In sum, Applicants therefore respectfully submit and maintain that the present Examiners have unfortunately misconstrued and misapplied the standards and facts needed for now imposing a Restriction Requirement for presently pending claims 1-15. Applicants respectfully affirm that claims 1-15 are intimately and directly related in sum and substance; that each of claims 1-15 recites similar requirements which

differ only incidentally in the details of the definition and not in the substantive essentials; and that all the presently pending claims constitute a single, yet broad invention which has been defined in the alternative to preserve the true scope and value of applicants' invention. Applicants further submit that there is no compelling reason for now demanding a Restriction of presently pending claims 1-15 in that all these claims have clearly been previously recognized and today remain alternative definitions of one, unified invention.

For all the reasons stated herein, applicants respectfully request that the present Examiners reconsider their position and withdraw the presently imposed Restriction Requirement completely and in its entirety. The Examiners are also invited to call applicants' undersigned attorney should they feel that such a telephone call would further the prosecution of the present application.

Respectfully submitted,

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